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Authors
Poisson, Sharon N
Glidden, David
Johnston, S Claiborne
et al.

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Deaths from stroke in US young adults, 1989–2009

Sharon N. Poisson, MD, MAS
David Glidden, PhD
S. Claiborne Johnston, MD, PhD
Heather J. Fullerton, MD, MAS

Correspondence to Dr. Poisson: Sharon.Poisson@ucdenver.org

ABSTRACT

Objective: To determine what the trends in stroke mortality have been over 2 decades in young adults.

Methods: In this cohort study, we analyzed death certificate data for ischemic and hemorrhagic stroke (intracerebral hemorrhage [ICH] and subarachnoid hemorrhage [SAH]) in adults aged 20–44 in the United States for 1989 through 2009, covering approximately 2.2 billion person-years. Poisson regression was used to calculate and compare time trend data between groups and to compare trends in young adults to those in adults over age 45.

Results: Mortality from stroke in young adults declined by 35% over the study period, with reductions in all 3 stroke subtypes (ischemic stroke decreased by 15%, ICH by 47%, and SAH by 50%). Black race was a risk factor for all 3 stroke subtypes (relative risk 2.4 for ischemic stroke, 4.0 for ICH, and 2.1 for SAH), but declines in all stroke subtypes were more dramatic in black compared to white participants ($p < 0.001$ for all stroke subtypes).

Conclusions: Although hospitalizations for stroke in young patients have been increasing, the apparent decrease in mortality rates and in racial disparities suggests that recognition and treatment in this group may be improving. ***Neurology*® 2014;83:2110–2115**

GLOSSARY

ICD-9 = *International Classification of Diseases–9*; ***ICD-10*** = *International Classification of Diseases–10*; **ICH** = intracerebral hemorrhage; **NCHS** = National Center for Health Statistics; **SAH** = subarachnoid hemorrhage.

Compared with older adults, ischemic stroke is relatively uncommon in young adults, comprising 5%–10% of all stroke.[1] However, because lifetime impacts are longer for strokes in younger adults, costs are substantial, both to the individual and to society. In contrast with the overall age-adjusted rate of stroke hospitalizations, which has been decreasing over the last 2 decades, some early studies suggest that stroke hospitalizations in young adults are rising over this same time period.[2–5] Trends in stroke mortality rates among young adults have not been well-studied. Given the reports of rising rate of strokes in this age group, we sought to better understand the trends in mortality from stroke in young adults. We also sought to determine whether race and sex differences previously described in the elderly were also present in young adults. Using death certificate data from the National Center for Health Statistics (NCHS), we examined the demographics and time trends of mortality from ischemic stroke, subarachnoid hemorrhage (SAH), and intracerebral hemorrhage (ICH) in young adults (aged 20–45 years) in the United States for 1989–2009.

METHODS We searched mortality databases of the NCHS to determine rates of death from stroke in young adults for 1989 through 2009. These databases contain information on primary cause of death as listed on death certificates in the United States. Cause of death in the database is coded by *ICD-9* code for the years up to 1998 and by *ICD-10* code from 1999 through 2009. For the earlier years, deaths due to stroke were identified using the following *ICD-9* codes[6–9]: for SAH, 430; for ICH, 431; and for ischemic stroke, 325, 433.x, 434.x, 436, 437.0, 437.1, 437.4, 437.5, and 437.6. For the later years, deaths due to stroke were identified using the following *ICD-10* codes[10,11]: for SAH, I60.x and I69.0; for ICH, I61.x and I69.1; for ischemic stroke, I63.x, I64, I67.0, I67.2, I67.5, I67.6, I67.7, I69.3, and G08; and for ill-defined cerebrovascular disease, I64, I69.4, and I69.8. Subtypes of ischemic stroke were ascertained from the following *ICD-9*/*ICD-10* codes in the earlier and later time periods, respectively: venous sinus thrombosis

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From the Department of Neurology (S.N.P.), University of Colorado Denver, Aurora; the Departments of Epidemiology and Biostatistics (D.G.) and Neurology and Pediatrics (H.J.F.), University of California San Francisco; and Dell Medical School (S.C.J.), University of Texas, Austin.

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(325, 437.6/G08, I67.6), infarction related to precerebral vessels (433/I63.0, I63.1, I63.2), infarction related to cerebral vessels (434/I63.3–I63.5), cerebral atherosclerosis/arteritis (437.0, 437.4/I67.2, I67.7), moyamoya (437.5/I67.5), cerebral infarction unspecified (I63.8, I63.9), dissection of cerebral arteries nonruptured (I67.0), sequelae of cerebral infarction (I69.3), and acute but ill-defined cerebrovascular disease (436/I64). There are prior data from a systematic review that *ICD-9* codes 433, 434, and 436 have higher positive predictive values (85% or higher) for ischemic stroke[12] compared with other codes, and that *ICD-10* codes I63 and I64 have similar accuracy.[10] Therefore we also calculated statistics for a more conservative estimate of ischemic stroke using these *ICD-9* codes for the earlier years and using *ICD-10* codes I63 and I64 for the later years. All analyses were done using both definitions of ischemic stroke.

Prior studies evaluating stroke in young adults have had variable age ranges, with minimum ages between 15 and 20 years and maximum age cutoff between 44 and 49 years. We chose to include all adults aged 20–45 years. Based on the ethnicity classification of the NCHS,[13] individuals were classified into 1 of 4 groups: black, white, American Indian or Alaska Native, or Asian or Pacific Islander. For the years prior to 1999, the NCHS mortality database grouped the latter 2 categories together as "other," so for comparability, we also grouped these categories for 1999 to 2009. Persons of Hispanic origin were considered to be "of any race" by this classification system; therefore, white Hispanics were classified as white and black Hispanics were classified as black. For the years prior to 1999, the database did not differentiate ethnicity, but Hispanic vs non-Hispanic ethnicity was included after 2009. We did a comparison of Hispanic and non-Hispanic ethnicity for 1999–2009, for which we have data. All population comparison information in the NCHS database is based on mid-year population estimates.

Death rates were calculated as the number of deaths per 100,000 people in a population. Age-, race-, and sex-specific population data were obtained from the US Census Bureau.[14,15] Person-years were defined as the total number of persons in a category multiplied by the number of years of study. Race-specific rates were age- and sex-adjusted.

Poisson regression was used to calculate time trend data and to compare trends between groups. In comparing trends between groups, interaction terms between stroke subtypes and year, race and year, ethnicity and year, sex and year, and age and year were included in the respective regression models. Year was treated as a discrete variable in all statistical analysis. For comparison, time trends for stroke mortality in older adults (≥45 years) were also analyzed using the same NCHS mortality database. Mortality rate ratios were calculated to determine differences between rates in different groups (averaged over entire time period). We used Stata (version 11.0, StataCorp, College Station, TX) for statistical calculations and graphical representation as well as Microsoft (Redmond, WA) Excel (version 14.2.1) for graphical representation.

Standard protocol approvals, registrations, and patient consents. This study did not meet requirements for human subjects research and therefore did not need approval by the institutional review board.

RESULTS About 2.2 billion person-years ages 20–44 years and 2.7 billion person-years ages ≥45 years were included in the study over the 21-year period (table 1). Whites accounted for 81% of the population in the young adults, and sex was evenly distributed. There were no significant differences in race or sex between the young adult and older adult populations ($p > 0.99$ for both). There were 59,077 deaths attributed to stroke in young adults in the United States from 1989 through 2009, yielding an average of 2,868 deaths per year. Ischemic strokes accounted for 25% of deaths, while hemorrhagic stroke accounted for 75% (table 2). The total number of deaths from stroke in adults ≥45 years was about 2.5 million, with 19% related to hemorrhagic stroke, 4% related to SAH, and 81% related to ischemic stroke. Average annual mortality rates among young adults were 0.93

Table 1 Demographic characteristics of total young adult and older adult population, 1989–2009

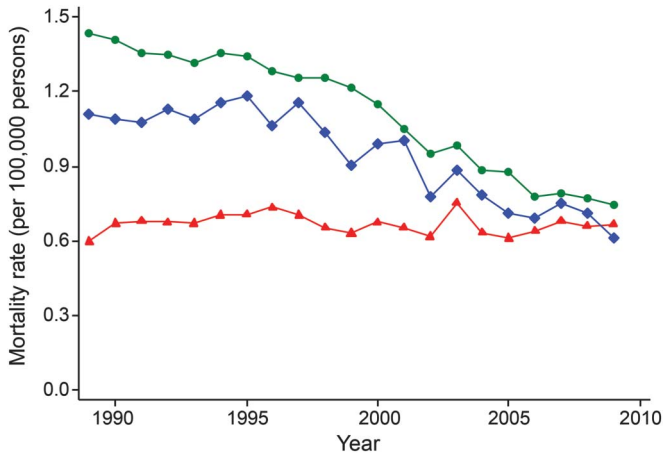
Young adults (aged 20–44 years)			Older adults (aged 45+ years)		
Characteristic	Person-years (total = 2,173,207,054)	Percent	Characteristic	Person-years (total = 2,742,245,074)	Percent
Race			Race		
Black	289,732,587	13	Black	266,547,766	10
White	1,757,356,873	81	White	2,380,233,357	87
Other	126,117,594	6	Other	95,463,951	3
Sex			Sex		
Female	1,079,874,614	50	Female	1,490,209,262	54
Male	1,093,332,440	50	Male	1,252,035,812	46
Age, y			Age, y		
20–24	411,671,205	19	45–54	978,541,527	36
25–34	866,928,485	40	55–64	755,797,805	28
35–44	894,607,364	41	65–74	560,435,217	20
			75–84	335,854,819	12
			85+	111,615,706	4

Table 2 Subtypes of stroke mortality among young adults and older adults, 1989–2009

	Young adults		Older adults	
Stroke types and subtypes	Deaths, n	% Total deaths	Deaths, n	% Total deaths
Intracerebral hemorrhage and sequelae	20,174	34	372,580	15
(*ICD-9* 431; *ICD-10* I61.x, I69.1)				
Subarachnoid hemorrhage and sequelae	23,960	41	109,782	4
(*ICD-9* 430; *ICD-10* I60.x, I69.0)				
Ischemic stroke				
Venous sinus thrombosis	182		258	
(*ICD-9* 325, 437.6; *ICD-10* G08, I67.8)				
Infarction related to precerebral vessels	584		10,889	
(*ICD-9* 433; *ICD-10* I63.0-I63.2)				
Infarction related to cerebral vessels	2,595		188,729	
(*ICD-9* 434; *ICD-10* I63.3-I63.5)				
Cerebral atherosclerosis/arteritis	364		50,321	
(*ICD-9* 437.0, 437.4; *ICD-10* I67.2, I67.7)				
Moyamoya	107		151	
(*ICD-9* 437.5; *ICD-10* I67.5)				
Cerebral infarction, unspecified	1,179		72,519	
(*ICD-10* I63.8, I63.9)				
Dissection of cerebral arteries, nonruptured	59		134	
(*ICD-10* I67.0)				
Sequelae of cerebral infarction	61		7,769	
(*ICD-10* I69.3)				
Acute, but ill-defined cerebrovascular disease	9,873		1,725,180	
(*ICD-9* 436; *ICD-10* I64)				
Subtotal	15,004	25	2,055,950	81
Total	59,138	100	2,538,312	100

Abbreviations: *ICD-9* = *International Classification of Diseases-9*; *ICD-10* = *International Classification of Diseases-10*.

Figure 1 Time trends in stroke mortality rate by stroke subtype in US young adults

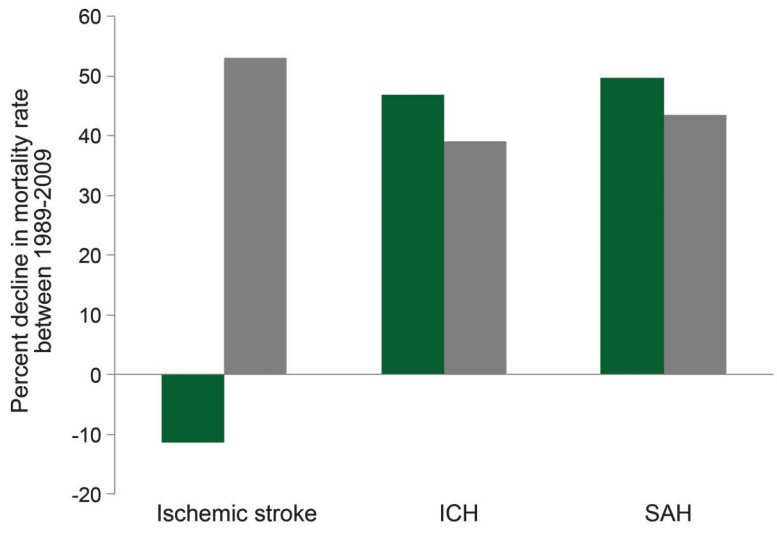


Circles represent subarachnoid hemorrhage, diamonds represent intracerebral hemorrhage, triangles represent ischemic stroke.

per 100,000 persons for ICH, 1.1 per 100,000 persons for SAH, and 0.70 per 100,000 persons for ischemic stroke. When ischemic stroke was defined more conservatively (*ICD-9* 433/434, *ICD-10* I63), the average annual mortality rate was similar, at 0.65 per 100,000 persons.

Between 1989 and 2009, mortality from overall stroke in young adults decreased by 38%, from 3.2 to 2.0 per 100,000 person-years. Mortality from ICH dropped 47% from 1.1 to 0.59 per 100,000 person-years and SAH dropped 50% from 1.4 to 0.7 per 100,000 person-years when comparing the rates at the beginning of the study to those at the end of the study (figure 1). The time trends for mortality from both types of hemorrhagic stroke were found to be significant ($p < 0.001$ for both). The rate of ischemic stroke (using the conservative definition), however, increased by 11% from 0.60 to 0.67 per 100,000 person-years. This trend, however, was

Figure 2 Percent decline in mortality rate from stroke subtypes in young adults and older adults



Green bar represents adults aged 20–44, gray bar represents adults aged 45 and older. ICH = intracerebral hemorrhage; SAH = subarachnoid hemorrhage.

not significant ($p = 0.338$). When using the less conservative definition of ischemic stroke, the increase over the 21-year period was 36%. Given the more conservative findings using the conservative definition, all further results are reported using the conservative definition of ischemic stroke.

When compared to adults aged 45 years and older, young adults had lower rates of all stroke subtypes. There were declines in the overall rates of ICH and SAH in both young and older adults, but the decline was more dramatic in young adults in both types of hemorrhagic stroke (figure 2). The time trends for the decline in mortality rates of ICH and SAH were significantly different when comparing age groups ($p < 0.001$ for ICH, $p = 0.003$ for SAH). The most striking difference was in ischemic stroke, where there was an 11% increase in the rate among young adults, but a 53% decline in adults ≥45 years. The time trend for ischemic stroke mortality was also significantly different ($p < 0.001$).

Among young adults, men were at higher risk than women of mortality from stroke overall, ischemic stroke, and ICH, but were at lower risk of death from SAH (table 3). Blacks had higher rates of mortality from all stroke subtypes, and from overall stroke. Person-time mortality rates for all stroke subtypes were highest in the 35–44 years age group, with rates of 12.4/100,000 person-years for ischemic stroke, 17.5 for ICH, 19.3 for SAH, and 49.9 for all stroke.

The decline in mortality from all stroke subtypes among young adults was more dramatic in blacks than in whites (figure 3). The time trend differences between blacks and whites were significant in all 3 subtypes ($p < 0.001$ for trend). The ratio of mortality in blacks to whites related to ischemic stroke dropped from 4.3/100,000 persons in 1989 to 2.4 in 2009, for ICH from 4.9 to 2.7, and for SAH from 2.4 to 1.6. From 1999 to 2009, there was no difference in the decline among Hispanics and non-Hispanics in ischemic stroke or ICH. The rate of SAH declined more slowly in Hispanics than in non-Hispanics, with a significant difference in trends ($p = 0.01$), and the rates of SAH converged by the end of the study. There were no differences between the trend in decline of mortality rates between men and women from ischemic stroke ($p = 0.21$) or SAH ($p = 0.90$). Rates of ICH mortality dropped more quickly in men than in women over the study period, with a significant difference in trend ($p = 0.006$). The rates of ICH mortality in 2009 among men (0.73/100,000 persons) and women (0.46/100,000 persons) were closer together, but did not converge.

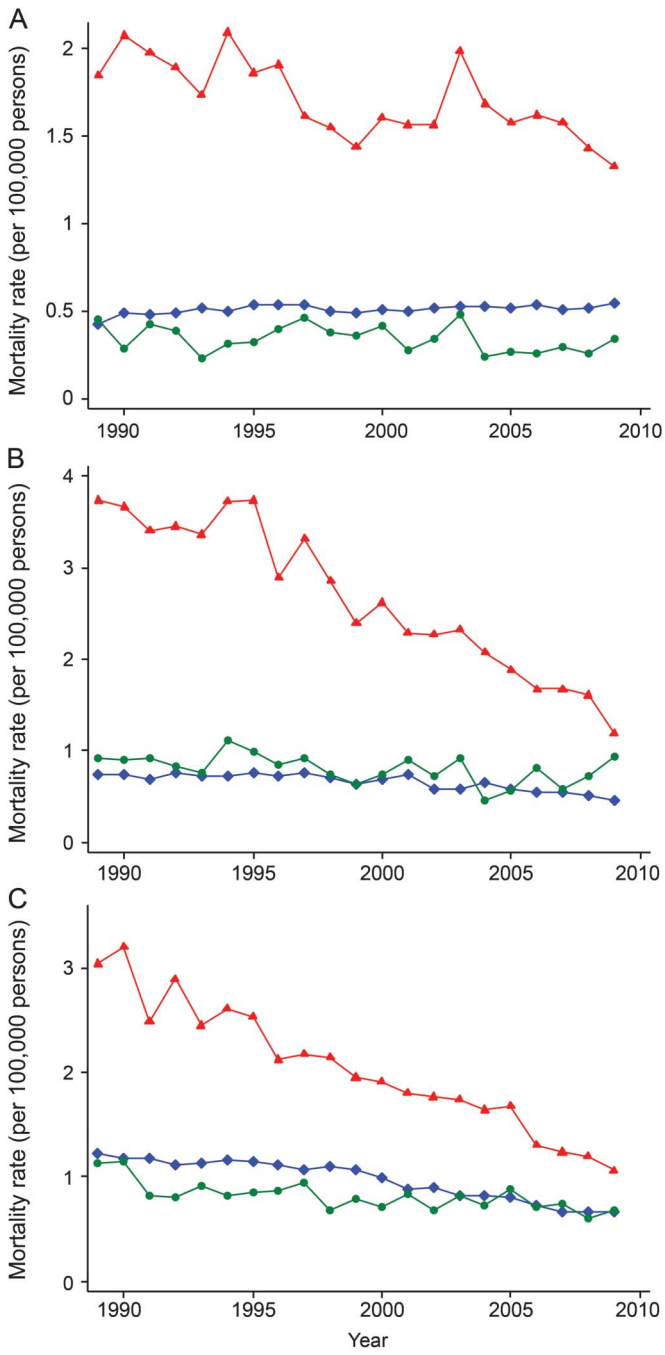
DISCUSSION Age-adjusted trends in stroke occurrence and stroke mortality are well-documented in older adults and have been declining significantly for several decades,[16] but have been less well-studied in young adults. We found that rates of mortality for hemorrhagic stroke subtypes have been declining in young adults over the last 2 decades, but ischemic stroke has not changed significantly, with a trend toward an increase. Mortality related to ICH and SAH has declined more among young adults than older adults, but despite a steep decline in ischemic stroke mortality among older adults, there has been a trend toward increasing rates in young adults.

Table 3 Demographics of young adult (<45 years) stroke mortality in the United States by stroke subtype, 1989–2009

	Mortality rate (deaths per 100,000 person-years)							
Stroke type	Male	Female	RR (male:female)	95% CI	Black	White	RR (black:white)	95% CI
Ischemic	7.1	5.9	1.2	1.1–1.2	16.9	5.1	3.3	3.2–3.5
ICH	10.9	7.7	1.4	1.4–1.5	26.2	6.6	4.0	3.9–4.1
SAH	9.6	12.4	0.8	0.7–0.8	20.0	9.7	2.1	2.0–2.1
All	27.9	26.6	1.1	1.0–1.1	64.0	21.8	2.9	2.9–3.0

Abbreviations: CI = confidence interval; ICH = intracerebral hemorrhage; RR = relative risk, calculated as the mortality rate ratio; SAH = subarachnoid hemorrhage.

Figure 3 Racial differences in time trends in mortality among US young adults by stroke subtype



(A) Ischemic stroke, (B) intracerebral hemorrhage, and (C) subarachnoid hemorrhage. Triangles represent black participants, diamonds represent white participants, and circles represent other.

Much of the improvement in ischemic stroke mortality among older adults is likely related to improved control of atherosclerotic risk factors, such as hypertension, hyperlipidemia, and smoking.[16,17] Traditionally, these risk factors have not been believed to play a major role in the etiology of stroke in the young, but there is increasing evidence that these risk factors are becoming more prevalent in this age group.[2,18,19] The dramatic decline in the SAH mortality rate, in particular, is likely linked to a decline in smoking, which has dropped 51% between 1945 and 2009.[20] The lack of a decline in ischemic stroke mortality among young adults could be, in part, related to the increasing prevalence of risk factors, but less aggressive treatment for prevention in this group compared with older adults. This lack of a decline in ischemic stroke mortality among young adults is consistent with the recent evidence that rates of hospitalization for ischemic stroke have been increasing over the last 2 decades.[2]

We found that among young adults, mortality from all stroke subtypes was higher among African Americans compared with whites, as is true in older adults[21] and in children.[22] However, we also found that declines in stroke mortality were greater over the 21-year study period in blacks, leading to a decreasing disparity. This narrowing of the differences may be related to the increased awareness of racial disparities in stroke, which has occurred in this same time period. Some recent evidence suggests that the incidence of hospitalization for ischemic stroke is increasing in this age group,[2,4] and that this trend was most apparent among blacks. Our findings suggest that despite the apparent increasing racial disparities in ischemic stroke incidence, the disparity is decreasing in mortality from ischemic stroke. The explanation for this difference is not clear, but could be related to the increasing awareness of stroke among blacks, and improved aggressive acute treatment.

Our findings that young men have higher rates of mortality related to ischemic stroke and ICH but women have higher SAH-related mortality parallel those seen in prior studies of overall adult stroke mortality.[23] The finding that young adults in the 35–44 years age group are at the highest risk of mortality from all 3 stroke subtypes is also not surprising, and likely reflects the higher incidence of all stroke subtypes in older age groups.

Our study has several limitations. Criteria for death certificate diagnoses are not clearly defined, and diagnoses may vary depending on diagnostic workup, physician, and administrator coding. In prior studies, however, discharge *ICD-9* codes for stroke, which we used, were found to be 98% sensitive for stroke in adults.[7] *ICD-10* codes have been found to be similarly accurate in coding stroke among adults.[10] Death certificate data have also been found to have high specificity and positive predictive value.[24] The NCHS data are limited by including only the primary diagnosis code from the death certificate, so we were unable to evaluate etiology of the strokes in this study. We did find a large percentage of patients with diagnostic codes that were nonspecific for stroke subtype. This limits our ability to evaluate the true mortality rates for each of the stroke subtypes.

Despite its limitations, this study provides important information about the trends in stroke mortality among young adults. Similar to trends in older adults, stroke mortality overall and among all of the subtypes is decreasing over time. Hemorrhagic stroke mortality trends are similar among young and older adults, although the difference in trends in ischemic stroke mortality is striking, and interesting especially in the face of recent data suggesting increasing incidence of ischemic stroke in this age group. Narrowing of the racial gap in stroke mortality suggests that increasing awareness of disparities may lead to better treatment, but further research needs to be done to improve our understanding of these trends.

AUTHOR CONTRIBUTIONS

Dr. Poisson was the PI for this study and was primarily involved in all aspects, including study design, data collection, data analysis, and manuscript preparation. Dr. Glidden was a biostatistical consultant, helping with the statistical analysis plan and interpretation, as well as revising the manuscript. Dr. Johnston helped with interpretation of the data as well as revisions of the manuscript. Dr. Fullerton was involved in the design of the study, interpretation of the data, and revision of the manuscript.

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DISCLOSURE

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REFERENCES

1. Biller J. Stroke: improving characterization of childhood cerebral arteriopathies. Nat Rev Cardiol 2009;6:395–397.
2. George MG, Tong X, Kuklina EV, Labarthe DR. Trends in stroke hospitalizations and associated risk factors among children and young adults, 1995–2008. Ann Neurol 2011;70:713–721.
3. Lehman L, Khoury J, Alwell K, et al. International stroke conference oral abstracts: Temporal trends in incidence and 30-day case fatality of pediatric stroke: a population-based study. Stroke 2010;41:e218.
4. Nguyen-Huynh MN, Emery MH, Sidney S. Abstract 10: Rising trend of ischemic stroke in the young. Stroke 2012; 43:A10.
5. Kissela B, Alwell K, Khoury J, et al. International stroke conference oral abstracts. stroke in the young is increasing over time: temporal trends in the age of stroke incidence in a large, bi-racial population. Stroke 2010;41:e224.
6. American Medical Association. International Classification of Diseases, 9th revision, clinical modification: *ICD-9-CM*. Chicago, IL: American Medical Association; 1999.
7. Broderick J, Brott T, Kothari R, et al. The Greater Cincinnati/Northern Kentucky Stroke Study: preliminary first-ever and total incidence rates of stroke among blacks. Stroke 1998;29:415–421.
8. Goldstein LB. Accuracy of *ICD-9-CM* coding for the identification of patients with acute ischemic stroke: effect of modifier codes. Stroke 1998;29:1602–1604.
9. Leibson CL, Naessens JM, Brown RD, Whisnant JP. Accuracy of hospital discharge abstracts for identifying stroke. Stroke 1994;25:2348–2355.
10. Kokotailo RA, Hill MD. Coding of stroke and stroke risk factors using *International Classification of Diseases*, revisions 9 and 10. Stroke 2005;36:1776–1781.
11. Anderson RN, Minino AM, Hoyert DL, Rosenberg HM. Comparability of cause of death between *ICD-9* and *ICD-10*: preliminary estimates. Natl Vital Stat Rep 2001;49:1–32.
12. Andrade SE, Harrold LR, Tjia J, et al. A systematic review of validated methods for identifying cerebrovascular accident or transient ischemic attack using administrative data. Pharmacoepidemiol Drug Saf 2012;21(suppl 1):100–128.
13. U.S. Census Bureau, Office of Management and Budget. Race and Ethnic Standards for Federal Statistics and Administrative Reporting. Statistical Policy Directive No. 15. Adopted May 12, 1977.
14. Centers for Disease Control and Prevention. CDC WONDER On-Line Database, Compiled From Compressed Mortality File CMF 1968–1988, Series 20, No. 2A, 2000 and CMF 1989–1998, Series 20, No. 2E, 2003. Available at: http://wonder.cdc.gov/cmf-icd9.html. Accessed December 3, 2013.
15. Centers for Disease Control and Prevention. CDC WONDER Online Database, Compiled From Compressed Mortality File 1998–2008, Series 20, No. 2N, 2011. Available at: http://wonder.cdc.gov/cmf-icd10.html. Accessed December 3, 2013.
16. Cooper R, Cutler J, Desvigne-Nickens P, et al. Trends and disparities in coronary heart disease, stroke, and other cardiovascular diseases in the United States: findings of the National Conference on Cardiovascular Disease Prevention. Circulation 2000;102:3137–3147.
17. Centers for Disease Control and Prevention. Decline in deaths from heart disease and stroke: United States, 1900–1999. MMWR Morb Mortal Wkly Rep 1999;48: 649–656.
18. Putaala J, Metso AJ, Metso TM, et al. Analysis of 1008 consecutive patients aged 15 to 49 with first-ever ischemic stroke: the Helsinki young stroke registry. Stroke 2009;40: 1195–1203.
19. Raiko JR, Viikari JS, Ilmanen A, et al. Follow-ups of the cardiovascular risk in Young Finns Study in 2001 and 2007: levels and 6-year changes in risk factors. J Intern Med 2010;267:370–384.
20. American Lung Association Research and Program Services Epidemiology and Statistics Unit. Trends in Tobacco Use. July 2011. Available at: www.lung.org/finding-cures/our-research/epidemiology-and-statistics-rpts.html.
21. Trimble B, Morgenstern LB. Stroke in minorities. Neurol Clin 2008;26:1177–1190.
22. Fullerton HJ, Wu YW, Zhao S, Johnston SC. Risk of stroke in children: ethnic and gender disparities. Neurology 2003;61:189–194.
23. Ayala C, Croft JB, Greenlund KJ, et al. Sex differences in US mortality rates for stroke and stroke subtypes by race/-ethnicity and age, 1995–1998. Stroke 2002;33:1197–1201.
24. Iso H, Jacobs DR Jr, Goldman L. Accuracy of death certificate diagnosis of intracranial hemorrhage and nonhemorrhagic stroke: the Minnesota Heart Survey. Am J Epidemiol 1990;132:993–998.